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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/006,922	12/04/2001	Sergey A. Lukyanov	CLON-035CIP	9351

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EXAMINER
ROBINSON, HOPE A

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 05/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

SUPPLEMENTAL **Office Action Summary**	**Application No.** 10/006,922	**Applicant(s)** LUKYANOV ET AL.	
	Examiner Hope A. Robinson	**Art Unit** 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,18-23,27 and 31-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,18-23,27 and 31-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. This is a Supplemental Office action because the Office action mailed on May 2, 2006 inadvertently did not address the newly submitted claims.

2. Applicant's response to the Office Action mailed December 15, 2005 on February 16, 2006, is acknowledged.

Claim Disposition

3. Claims 1-13, 18-23, 27 and 31-62 are pending and are under examination.

Withdrawn-Specification Objections

4. Previous objection to the specification regarding the abstract, title, priority information and sequence notations are withdrawn by virtue of submission of an amendment.

Withdrawn-Objection to Claims

5. Previous objection to claims are withdrawn by virtue of submission of an amendment.

Withdrawn-Claim Rejections - 35 USC э 101

6. Previous rejection to claims under 35 U.S.C. 101 is withdrawn by virtue of submission of an amendment, which cancelled the claims.

Maintained and Amended-Claim Rejections - 35 USC ∋ 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-13, 18-23, 27 and 31-62 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is directed to a nucleic acid present in other than its natural environment that encodes a chromo or fluorescent protein wherein said protein has a sequence identity of at least 70%, 75%, 80% or 85% sequence identity to SEQ ID NO:12. This represents a partial structure and a skilled artisan would not be able to envision the detailed chemical structure of the genus of proteins encompassed the claims. There is no indication in the claims or specification as to where in the claims modifications will occur. Thus, the instant specification fails to provide adequate description for the large genus of proteins encompassed in the claims. The claims encompass mutations other than point mutations or single deletions, which have not been described. The specification fails to provide a representative number of species for the claimed genus to show that applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described, are representative of

the entire genus. In addition, the claims recite that said nucleic acid encodes a protein that has one or more amino acid substitutions selected from amino acid substitutions at positions 2, 5, 9, 105 or 197 as compared to SEQ ID NO:12. The language in the claim is open as "has" is interpreted as "comprising" and the phrase "one or more amino acid substitutions" does not place a limit on whether position 2 for example, will have 1 or 5 or 10 or 15 substitutions or describe the possible combinations. Additionally, the claimed invention is directed to "one or more amino acid substitutions selected from R2A, K5E, K9T, V105A and S197T". A genus of mutations are encompassed in this claim language, for example the following combinations can occur and a lot more: (a)R2A, K5E, K9T, V105A, S197T; (b)R2A, K5E ; (c)R2A, K9T; (d)R2A,V105A; (e)R2A, S197T; (f) K5E, K9T; (g)K5E, V105A; (h)K5E, S197T; (i)K9T, V105A; K9T, S197T; (j)V105A, S197T; (k)R2A, K5E, K9T; (l)R2A, K5E, V105A; (m)R2A, K5E, S197T; (n)K5E, V105A, K9T. The instant specification on page 6 discloses that "[T]he proteins of interest are proteins that are colored and/or fluorescent, where this feature arises from the interaction of two or more residues of the protein". The specification does not provide adequate written description of which two or more residues results in the desired effect and as demonstrated above the claimed invention encompasses a genus of mutants based on the recited "one or more substitutions". A skilled artisan would have to determine which two point mutations or combination of mutations will produce the desired effect/interaction. Therefore, the claimed invention lacks adequate written description for the genus of proteins encompassed in the claims.

Further, *Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir.1991)*, states that "applicant must convey with reasonable clarity to those skilled in the

art that, as of the filing date sought, he or she was in *possession of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of proteins encoded the claimed nucleic acid, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. *See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993).*

Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

8. Claims 1-13, 18-23, 27 and 31-62 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the nucleic acid set forth in SEQ ID NO: 11 that encodes the protein set forth in SEQ ID NO:12 and specific point mutations exemplified in the specification, does not reasonably provide enablement for any fragment thereof or a transgenic organism or progeny thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The enablement requirement refers to the requirement that the specification describe how to make and how to use the invention. There are many

factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: Quantity of Experimentation Necessary; Amount of direction or guidance presented; Presence or absence of working examples; Nature of the Invention; State of the prior art and Relative skill of those in the art; Predictability or unpredictability of the art and Breadth of the claims (see *In re Wands, 858 F.2d at 737, 8 USPQ2d at1404 (Fed. Cir. 1988)*. The factors most relevant to the instant invention are discussed below.

The amount of experimentation required to practice the claimed invention is undue as the claims encompass an unspecified amount of fragments. The claimed invention is directed to a nucleic acid present in other than its natural environment encoding a protein having a sequence identity of at least about 70-85% to SEQ ID NO:12. No guidance is provided in the instant specification as to any special feature/characteristics or the structure of all the possible fragments encompassed by the claims. There are no indicia as to how much modifications can be tolerated in the wild type structures. The claims encompass mutations that are not limited to a single point mutation and encompass a large variable genus of proteins. In addition, newly submitted claims 53-62 recite that said nucleic acid encodes a protein that has one or more amino acid substitutions selected from amino acid substitutions at positions 2, 5, 9, 105 or 197 as compared to SEQ ID NO:12 and the claims are also directed to "one or more amino acid substitutions selected from R2A, K5E, K9T, V105A and S197T compared to SEQ ID NO:12". The language in the claim is open as "has" is interpreted as "comprising" and the phrase "one or more amino acid substitutions" does not place a limit on whether position 2 for example, will have 1 or 5 or

10 or 15 substitutions or describe the possible combinations (see for example claim 53). Furthermore, a genus of mutations are encompassed in the claim language (see claim 54), for example the following combinations can occur and a lot more: (a)R2A, K5E, K9T, V105A, S197T; (b)R2A, K5E ; (c)R2A, K9T; (d)R2A,V105A; (e)R2A, S197T; (f) K5E, K9T; (g)K5E, V105A; (h)K5E, S197T; (i)K9T, V105A; K9T, S197T; (j)V105A, S197T; (k)R2A, K5E, K9T; (l)R2A, K5E, V105A; (m)R2A, K5E, S197T; (n)K5E, V105A, K9T. Note that the instant specification on page 6 disclose that "[T]he proteins of interest are proteins that are colored and/or fluorescent, where this feature arises from the interaction of two or more residues of the protein". The specification does not provide adequate guidance as to which two or more residues results in the desired effect and as demonstrated above the claimed invention encompasses a genus of mutants based on the recited "one or more substitutions". No correlation is made between structure and function of the encoded protein. A skilled artisan would have to perform undue experimentation to construct all the claimed fragments absent guidance.

The instant specification does not demonstrate or provide guidance as to what the structure of the protein will be once modified based on the changes contemplated in the claims and the instant specification (i.e. 70-85% sequence identity). Based on vast amount of modifications encompassed in the claims said nucleic acid might encode a protein that is non-functional or different. Additionally, there is no data provided demonstrative of a particular portion of the structure that must be conserved. One skilled in the art would have to engage in undue experimentation to construct for example, a fragment thereof and then produce from this a chromo protein or fluorescent protein that maintains the recited properties. Due to the large quantity of experimentation necessary to generate the infinite number of fragments recited in the

claims and possibly screen same for activity/desired properties and the lack of guidance/direction provided in the instant specification, this is merely an invitation to the skilled artisan to use the current invention as a starting point for further experimentation. Thus, undue experimentation would be required for a skilled artisan to make and/or use the claimed invention commensurate in scope with the claims.

Predictability of which potential changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved and detailed knowledge of the ways in which the protein's structure relates to its function. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, for example, multiple substitutions. In this case, the necessary guidance has not been provided in the specification. Therefore, while it is known in the art that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited, as certain positions in the sequence are critical to the protein's structure/function relationship. It is also known in the art that a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many cases. For example, various sites or regions directly involved in binding activity and in providing the correct three-dimensional spatial orientation of binding and active sites can be affected (see Wells, Biochemistry, vol. 29, pages 8509-8517, 1990). It is in no way predictable that randomly selected mutations, such as deletions, substitutions, additions, etc., in the disclosed sequences would result in a protein having activity/properties comparable to the

one disclosed. As plural substitutions for example are introduced, their interactions with each other and their effects on the structure and function of the protein is unpredictable. It is noted that the instant specification provides for example point mutations, however, the claims encompass plural substitutions, which are not exemplified, nor are there examples of all the possible mutant sequences. Thus, the skilled artisan would recognize the high degree of unpredictability that all the fragments/mutants encompassed in the claims would retain the recited properties.

The state of the prior art provides evidence for the high degree of unpredictability as stated above. For example, Heim et al. (PNAS, vol. 91, pages 12501-04, 1994) disclose that a mutated DNA was sequenced and found to contain five amino acid substitutions, only one of which was found to be critical, Tyr66His, in the center of the chromophore. Heim et al. also disclose further site directed mutagenesis and noted that there was tolerance of the substitutions made, however, some mutants were weakly fluorescent (page 12504). Therefore, amino acid substitutions are critical to the protein's structure/function relationship.

The specification lacks adequate guidance/direction to enable a skilled artisan to practice the claimed invention commensurate in scope with the claims. Furthermore, while recombinant and mutagenesis techniques are known in the art, it is not routine in the art to screen large numbers of fragments where the expectation of obtaining similar activity is unpredictable based on the instant disclosure. Moreover, the amino acid sequence of a protein determines its structural and functional properties, and predictability of what mutations can be tolerated in a protein's sequence and result in certain activity/property, which is very complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's function

from mere sequence data are limited, therefore, the general knowledge and skill in the art is not sufficient, thus the specification needs to provide an enabling disclosure.

The working examples provided do not rectify the missing information in the instant specification pertaining to the claimed mutants/fragments as the claims encompass mutants/fragments not described in the instant specification. Thus, one of skill in the art would have to engage in undue experimentation to construct the mutants/fragments of the claimed invention and examine the same for function/the specific properties.

The specification does not provide support for the broad scope of the claims, which encompass an unspecified amount of fragments. The claims broadly read on a whole organism and a transgenic cell or organism, for example a human for which no support is provided in the instant specification. The issue in this case is the breath of the claims in light of the predictability of the art as determined by the number of working examples, the skill level artisan and the guidance presented in the instant specification and the prior art of record. This make and test position is inconsistent with the decisions of *In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)* where it is stated that "...scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988)*. Therefore, the instant specification to be enabling need to provide direction/guidance regarding whether the structure of the chromo or fluorescent fragment/mutant can tolerate the modifications encompassed by claims and still possess the desired properties or whether a

protein that does not have the desired properties may result. Absent sufficient guidance/direction one of skill in the art would not be able to practice the claimed invention commensurate in scope with the claims.

Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention as the amount of experimentation required is undue, due to the broad scope of the claims, the lack of guidance and insufficient working examples provided in the specification and the high degree of unpredictability as evidenced by the state of the prior art, attempting to construct and test mutants of the claimed invention would constitute undue experimentation. Making and testing the infinite number of possible fragments to find one that has the desired properties as described is undue experimentation. Therefore, applicants have not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner that reasonably correlates with the scope of the claims, to be considered enabling.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

9. Claims 22-23 and 27 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter, which applicant (s) regard as their invention.

Claim 22 as amended lack clear antecedent basis for the recitation of "a nucleic acid selected from the nucleic acids according to claim 1" because claim 1 recites "a nucleic acid". The dependent claim hereto is also included as they do not rectify the situation.

Claim 27 as amended lack clear antecedent basis for the recitation of "selected from the nucleic acids according to claim 1" because claim 1 recites "a nucleic acid".

Withdrawn-Claim Rejections - 35 USC § 102

10. Previous rejection of claims 1-5, 8-10, 12-23, 27 and 31 rejected under 35 U.S.C. 102(b) is withdrawn by virtue of submission of an amendment.

Response to Arguments:

11. Applicant's response filed on February 16, 2006, January 13, 2006 and September 27, 2005 has been considered. Note that the objections of record have been withdrawn. Applicant's comments regarding the interview on January 4, 2006 is noted. Note that the rejections of record remain, except for the rejection under 35 U.S.C. 101 and 102. Note also that two rejections remain under 35 USC 112, 2nd paragraph because the amendments made to claims 22 and 27 were insufficient to over come the rejection of record. The dependent claims read on "nucleic acids" and the independent claim reads on "a single nucleic acid". Thus the rejection remains, although amended to reflect changes to the claims.

The rejections under 35 U.S.C. 112, first paragraphs have been amended to reflect changes made to the claims or arguments presented. Applicant's arguments pertaining to the rejection under 35 U.S.C. 112, first paragraph enablement were considered, however are not persuasive. Applicant on pages 10-11 of the amendment filed on January 13, 2006, state that the Shaner et al. reference published November 21, 2004 as well as alignments of the Shaner et al. reference compared to SEQ ID NO:12 provide evidence for the fragments claimed as the Shaner

et al. reference has proteins at least 80% identical to SEQ ID NO:12 of the instant application. It is also stated that "it is well established decisional law that all available evidence of enablement of an application as of its filing date must be considered, whenever that evidence becomes available, including after the filing date. *In re Hogan, 194 USPQ 527, 537 (CCPA 1977)*". This argument is not persuasive. The MPEP states that "[I]n certain circumstances, references cited to show a universal fact need not be available as prior art before applicant's filing date. In re Wilson, 311 F.2d 266, 135 USPQ 442(CCPA 1962). Such facts include the characteristics and properties of a material or a scientific truism. Some specific examples in which later publications showing factual evidence can be cited include situations where the facts shown in the reference are evidence "that, as of an application 's filing date, undue experimentation would have been required, In re Corneil, 347 F.2d 563, 568, 145 USPQ 702, 705 (CCPA 1965), or that a parameter absent from the claims was or was not critical, In re Rainer, 305 F.2d505, 507 n.3, 134 USPQ 343, 345 n.3 (CCPA 1962), or that a statement in the specification was inaccurate, In re Marzocchi, 439 F.2d 220, 223 n.4, 169 USPQ 367, 370 n.4 (CCPA 1971), or that the invention was inoperative or lacked utility, In re Langer, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA 1974), or that a claim was indefinite, In re Glass, 492 F.2d 1228,1232 n.6, 181 USPQ 31, 34 n.6 (CCPA1974), or that characteristics of prior art products were known, In re Wilson, 311 F.2d 266, 135 USPQ 442 (CCPA 1962)." In re Koller, 613 F.2d 819, 823 n.5, 204 USPQ 702, 706 n.5 (CCPA 1980) (quoting In re Hogan, 559 F.2d 595, 605 n.17, 194 USPQ 527, 537 n.17 (CCPA 1977) (emphasis in original)). However, it is impermissible to use a later factual reference to determine whether the application is enabled or described as required under 35 U.S.C. 112, first paragraph. In re Koller, 613 F.2d 819, 823 n. 5, 204 USPQ 702, 706 n.5 (CCPA 1980).

References which do not qualify as prior art because they postdate the claimed invention may be relied upon to show the level of ordinary skill in the art at or around the time the invention was made. Ex parte Erlich, 22 USPQ 1463 (Bd. Pat. App. & Inter. 1992) see MPEP chapter 2100, emphasis added. Thus, applicant's statements that evidence can be provided whenever it becomes available to provide support for enablement and written description is inaccurate. Furthermore, the Shaner et al. reference is said to enable 80% sequence identity, however, the claimed invention is directed to 70%, 75% and "at least about 80%. Note that the instant specification does not provide a definition of the term "at least about", and the broadest reasonable interpretation of that language is "at least" means "no less than or as a minimum" and "about" means "an approximation". Thus, "at least about 80%" can be interpreted as 78% or 79%. Therefore, the Shaner et al. reference is inadequate to enable the claimed invention as it is post-filing evidence and does not demonstrate all the fragments claimed.

The response filed on September 27, 2005 on pages 18-20 argue that the courts permit some experimentation and that extensive experimentation is not undue. This argument is not persuasive. While the instant specification describes and enables 10 variants as stated in the response on page 20 (filed September 27, 2005) and provides a discussion of methods to make others, these methods do not enable one of skill in the art to make all, or a relevant portion of, the proteins and polynucleotides within the scope of the claims. No description in the specification or the art provides particular residues whose encoding is important within the disclosed sequence so that the protein's properties is maintained. Thus, one of skill in the art would be unable to predict the structure of the other members of the genus in order to make such members. While it is known in the art that many amino acid substitutions are possible in any given protein, the

positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited, because certain positions in the sequence are critical to the protein's structure/function relationship. Further, the art recognizes that an amino acid change can destroy the function of the protein in many cases. For example, various sites directly involved in binding activity, oligomerization, active site catalysis and the three-dimensional structure can be affected. No correlation is made between structure and function for the variants encompassed in the claims. The instant specification provides no guidance/direction as to which regions of the protein would be tolerant of modifications and which would not. It is in no way predictable that randomly selected mutations, such as deletions, substitutions, insertions, etc., in the disclosed sequence would result in a protein having activity comparable to the one disclosed. While recombinant and mutagenesis techniques are known in the art, it is not routine in the art to screen large numbers of mutated proteins where the expectation of obtaining similar activity is unpredictable based on the instant disclosure. The amino acid sequence of a protein determines its structural and functional properties, and predictability of what mutations can be tolerated in a protein's sequence and result in certain activity. This is very complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's function from mere sequence data are limited. In addition, note that the newly submitted claims do not rectify the issues raised because the new claims also encompass a genus of proteins not supported by the instant specification. Thus, the rejection remains for the reasons stated above and herein.

Regarding the written description rejection, the applicant on pages 11-12 of the amendment filed on January 13, 2006 state that " compliance with the written description

requirement is essentially a fact-based inquiry that will necessarily vary depending on the nature of the invention claimed. Applicant also cites *Capon v. Eshhar; Amgen, Inc. v. Hoechst Marion Roussel, Inc.* and *Bilstad v. Wakalopulos*. In addition, it is stated that "sufficient written description for one with knowledge and skill in this particular art to recognize that Applicants were in possession of their generic invention without the need for an exhaustive disclosure of additional representative embodiments. Furthermore applicant state that, Shaner et al. paper published after Applicant's filing date, not only validates statements made in Applicant's statements, but also in so doing shows predictability in this art". Applicants also state that because "Applicant's disclosure is enabling for the full scope of their claims, the written description requirement is *ipso facto* satisfied as well".

These arguments have been considered but are not persuasive. As stated above the Shaner et al. paper does not qualify as evidence for enablement or written description based on the fact that it was filed after the filing date of the instant application. Applicant has not demonstrated possession of the genus of proteins encompassed in the claims at the time of filing. The specification does not provide any information as to where in the claimed sequence changes will occur, if the modifications result in contiguous/sequential run of residues, what regions are conserved or the composition of amino acids in the resulting sequence (i.e. a structure for the fragments). The written description guidelines requires that a representative number of species of the claimed genus is provided to show that applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described, are representative of the entire genus. A skilled artisan cannot envision the detailed chemical structure of the encompassed genus of proteins encoded by the claimed nucleic acid and

therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. *See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993).*

The response filed on September 27, 2005 on pages 17-18 state that the language in the claims was amended to expedite prosecution by adding "nucleic acids encode a protein that has an amino acid sequence that is at least 70% identical to the sequence of SEQ ID NO:12", and applicant assert that the specification provides adequate written description and support for such a claim. This argument is not persuasive as the claims only provide a partial structure and encompass a genus of proteins with the recited "70% identity". Applicant points to the instant specification at pages 56-57, Table 10 (and Fig 16 page 47, line 35 to page 53, line 20) as providing variants of the claimed sequence. Note that the mutants exhibited are primarily point mutations. The instant claims are not limited to said mutants, claim 1 for example broadly reads, at least about 70% with SEQ ID NO:12 which encompassed more variants than exemplified in the instant specification, for which no description is provided. Note that the newly submitted claims are also rejected herein because the genus of proteins encompassed in the claims, are not adequately described. Thus, the rejection remains for the reasons of record and stated herein.

Conclusion

12. No claims are allowable.

13. Applicant's amendment necessitated the new/modified ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr, can be reached at (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope Robinson, MS

Patent Examiner 5/16/06

HOPE ROBINSON
PATENT EXAMINER